PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
501564/MAW/nlp		
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU2003/000735	13 June 2003	13 June 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] A61K 038/17; A61P 25/16, 25/28

Applicant

UNIVERSITY OF TASMANIA et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of the report
22 December 2003	17 September 2004
Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**MICHAEL GRIEVE** Telephone No. (02) 6283 2267

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000735

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1 to 17, 26**	**YES**
	Claims **18 to 25, 27**	**NO**
Inventive step (IS)	Claims	**YES**
	Claims **1 to 27**	**NO**
Industrial applicability (IA)	Claims **1 to 27**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

D1: US 5,268,175A

D2: US 5,431,923A

D3: FR 2813529

D4: WO 1998/031795A

D5: WO 2002/043507A

D6: Anal Bioanal Chem Vol.372(3) (2002) pages 412 to 417

D7: J Am Geriatr Soc Vol.38(6) (1990) pages 633 to 639

D8: Neurobiology of Disease Vol.5(5) (1998) pages 349 to 356

D9: Journal of Chemical Neuroanatomy Vol.15(1) (1998) pages 21 to 26

D10: The FASEB Journal Vol.10(10) (1996) pages 1129 to 1136

NOVELTY (N)

The invention as claimed in Claims 18 to 25 and 27 fail to meet the criteria set out in PCT Article 33(2) as lacking novelty in light of the disclosure of documents D1 to D4. These documents disclose therapeutic compositions adapted for the topical application of metallothionein isoform MT-IIA as the active ingredient, optionally in combination with metallothionein isoform MT-I, MT-II, MT-III and/or MT-IV (please note that the present compositions are not construed as being limited to the treatment of neuronal compromise, but must merely be suitable for this use).

INVENTIVE STEP (IS)

The present Claims 1 to 27 are considered to lack an inventive step under PCT Article 33(3) in light of documents D5 to D10 when combined with documents D4. Documents D5 to D10 disclose that neuronal disorders and conditions such as Alzheimer's disease are caused by metallothionein (MT) imbalances (in particular, MTs store and release essential [heavy] metals within the body, maintaining low intracellular concentrations of said essential metals. The prior art suggests that MTs may be downregulated in conditions such as Alzheimer's disease, resulting in increased essential metal concentrations). Document D5, in particular, relates to the treatment of Alzheimer's and neuronal disorders via the administration of a supplement which increases the production of MT within the body, rather than the administration of MT itself.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Document D4, however, relates to the administration of a topical formulation of MT in the treatment of heavy metal poisoning. The problem to be solved by the present invention resides in the use of metallothionein isoform MT-IIA compounds in the stimulation of neuronal growth or repair, in order to treat neuronal disorders and conditions such as Alzheimer's disease. Therefore, in light of the above disclosures, a Person Skilled in the Art would be led to determine if the topical administration of MT, known to be effective in the treatment of heavy metal poisoning, would also be effective in the treatment of neuronal disorders and conditions such as Alzheimer's disease (caused by imbalances in essential [heavy] metal concentrations in the body), without the use of an inventive step.